DATA EVALUATION RECORD

STUDY 9

CHEM 112600   Prohexadione calcium   §164-1
CAS No. 127277-53-6
FORMULATION-00-ACTIVE INGREDIENT

STUDY MRID 44725213
Jackson, S. H., Wesley, D.S., and J.R. Patel. November 25, 1998. Amended Final Report: Field dissipation of BAS 125 W in orchard use patterns - NY, CA, and OR. Submitted by BASF Corporation. RTP, NC. BASF Reg. Document No. 98/5199 and Protocol No. 96015 (Amended Final Report). 3 volumes, 1070 pp.

REVIEWED BY :   Iwona L. Maher, Chemist
                 Environmental Risk Branch 1/EFED

SIGNATURE: _Iwona Maher_

DATE: 7/26/2000

APPROVED BY: James A. Hetrick, Ph.D., Chemist
                 Environmental Risk Branch 1/EFED

SIGNATURE: _James A. Hetrick_

DATE: 7/26/2000

<u>CONCLUSIONS</u>:
<u>Field Dissipation - Terrestrial</u>

1. This study is scientifically valid and marginally acceptable for the fulfillment of the data requirement for a terrestrial field dissipation study for prohexadione calcium on orchard use (apples and pears). This study shows that prohexadione calcium (BAS 514H) dissipated with EFED calculated non-linear first order kinetics half-lives of 15, 20, and 5.7 days in the NY, CA, and OR bare soil plots, respectively, following two treatments of 2.0 lb a.i./acre of prohexadione calcium broadcast of 14 day intervals. Prohexadione calcium residues were detected at a depth of 6-12" inches in the CA (one replicate of 0.017 ppm at 10 days after 2nd application), OR (two replicates of 0.067 ppm at 2 days after 1st application and 0.019 ppm at 10 days after 2nd application), and NY sites (one replicate of 0.015 ppm at 1 day after 1st application, see The Reviewer's Comments 2), at the concentration levels above the LOQ (0.01 ppm). No residues were detected below 12 inches at concentrations ≥ 0.01 ppm. Residues of despropionyl (KI-5376) were detected at a maximum concentration of 0.055 ppm at the 0-3" inch depth at 2 days after the 2nd application in CA site.

2. This study is marginally acceptable because the major degradate was not stable in the freezer storage. Because of the instability of the degradate in the freezer storage the study does not provide useful quantitative data to assess the fate and transport of the degradate.

3. The authors stated that prohexadione dissipation was due to degradation in soil. They proposed that prohexadione calcium degrades to despropionyl which degrades further into tricarballylic acid and citric acid, both naturally occurring substances. The two acids are subsequently mineralized to CO_2, a major terminal product.

4. The half-lives in these field dissipation studies are longer than expected from the laboratory study findings (the aerobic soil metabolism nonlinear half-life, $t_{1/2}$, was1.4 days with $r^2 = 0.98$, while the linear $t_{1/2}$ was 9.8 days with $r^2 = 0.73$; MRID 44457785). Most likely it is due to multiple processes occurring simultaneously in the field, perhaps soil moisture differences, and collection of very scattered data suggesting insufficient sample size to obtain representative results, and/or nonuniform prohexadione calcium application.

5. No further information is needed on the terrestrial field dissipation of prohexadione calcium at the present time, however, if dyspropionyl is identified as of toxicological concern than additional data on the degradate will be required.

METHODOLOGY:

Test Substance: BAS 125 06 W 27.5% DF, 28.6% w/w calcium 3,5-dioxo-4-propionyl-3-cyclohexenecarboxylate purity determined by GLP analysis, lot no. AF284-88.

Field Site and Application of Test Material: The field trial study was conducted at three sites in New York (on a Oakville soil in Wayne County northwest from North Rose; loamy sand: 0-6" soil depth composed of 78% sand, 17% silt, 5% clay,and 2.9% OM), California (on a San Joaqin soil in Tulare County several miles south from Porterville; clay loam: 0-6" soil depth composed of 36% sand, 34% silt, 30% clay,and 2.1% OM), and Oregon (on a Woodburn silt loam soil series in Marion County near the Woodburn town; 0-6" soil depth composed of 30% sand, 51% silt, 19% clay,and 2.3% OM). The NY site was chosen to represent the northeastern, mostly rainfed, agriculture area. The CA site represented the typical southwestern 100% irrigated agriculture area, and the OR site was chosen to represent the northwestern agricultural area which is both rainfed and inrrigated. All bareground soil received two 2.04 lb ai/A applications (120% label rate) at a 14 day interval (NY at 8/05/96 and 8/19/96; CA at 8/13/96 and 8/27/96; OR at 8/10/96 and 8/24/96; 59 and 45 days prior to harvest). BAS 125 06 W at 40 GPA water spray volume was broadcast using a tractor mounted boom sprayer. To supplement natural precipitation, irrigation was applied to the plots as needed.

Metorological Conditions: In Appendix B Tables 5 and 6 present average monthly air temperatures and precipitation data, respectively.

Soil Sampling: From the treated plots three replicate composites of 5 soil cores (A, B, and C) 0" to 48" depth were collected before and after each application, 1, 2, and 3 days after the first application, and 1, 2, 3, 4, 5, 7, 10, 14, 21, 30, 60, 90, 120, 180, 300, and 360 days after the last application. There were occasional variences in the sample collection days in samples collected after 30 days from the last application. From the control plots cores were collected before and after each application, at 2, 30, 90, 180, and 300 days after the last application.

Application Verification: A compound application verification was conducted using a petri dish. Fifteen 100 mm petri dishes containing 10 grams of sieved untreated soil were placed randomly in the bare soil plots before applications and collected immediately after. They were analyzed as 5 composites of three together with three spiked composites and three control perti dish composites. The samples were analyzed by ADPEN Laboratories, Inc. (p 860 results) In the field, soil samples were transferred from petri dishes to glass amber bottles using DW adjusted to pH 9 with NaOH. The soil samples were extracted with ammonium bicarbonate in a shaker at 200-300 rpm and 50 °C for an hour. The extract was filtered through a #4 filter, diluted to known volume with pH 9 water, diluted in 1% acetic acid (1:50 to 1:100) and analyzed via HPLC/UV. MDL was 295 ug of BAS 125 W in the sample. To validate application zero-time core recovery and a sprayer-calibration/pass time method were also used. Zero-time cores were defined as the first sample collected after the application to the plot and their concentrations were

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calculated by subtracting BAS 125 W residue in the 0-3" core before last application from the residue after the last application.

Soil Core Analysis: Soil cores were analyzed in all soil depths until two residue free depths were obtained. The soil samples were analyzed for BAS 125 W and its metabolite, despropionyl-prohexadione, using high performance liquid chromatography with an ultraviolet detection technique (HPLC/UV detector, BASF Analytical Method No D9607). BAS 125 W and despropionyl were extracted twice from soil samples (20g) by shaking with 0.1 N ammonium bicarbonate in a speed shaker (30 min, at 300 rpm, 50 °C). The combined extracts were centrifuged to remove solids. The obtained supernatants were acidified and cleaned-up using SAX SPE column. The prohexadione residues were eluted with pH-2 water under vacuum conditions. The eluate was devided into two equal aliquots. One aliquot was processed for prehexadione calcium and the second for despropionyl. One aliquot was three times extracted with ethyl acetate after the addition of concentrated sulfuric acid (4 ml) and sodium chloride (20 g). The ethyl acetate extract was filtered with a PS-1 filter with sodium sulfate (50 g). The filtrate was dried, redissolved in 1% acetic acid, and analyzed for prohexadione calcium via HPLC/UV with column switching.

After adjusting pH to 7-8 with 0.5 N sodium hydroxide, the second aliquot was cleaned-up using ENV+SPE column. The despropionyl residue was eluted from column with water (25 ml) under vacuum. The purified eluate's pH was adjusted to pH 2 with sulfuric acid and the eluate was cleaned-up again via ENV+SPE column. The column was eluted with ethyl acetate (15 ml). The obtained eluate was extracted twice with 0.5 N sodium hydroxide. The aqueous fraction was diluted to 10 ml, acidified to at least pH 2, and analyzed for despropionyl (KI-5376) via HPLC/UV (column switching).

All soil sample residues were corrected for soil moisture content but were not corrected for procedural recoveries. This method assures 79.3 ± 9.0% (n=281) average procedural recoveries of BAS 125 W in soil, 82.7 ± 10.4% (n=286) of prohexadione, and.73.5 ± 10.4% (n=530) of despropionyl. For this method the limit of quantitations (LOQ) are 0.01 ppm for both BAS 125 W and its degradate despropionyl.

Sample Storage and Stability: Soil samples were shipped in a freezer truck to BASF Corporation in RTP, NC. After processing the sample aliquots were shipped frozen, in insulated containers with dry ice, from BASF to ADPEN Laboratory for analysis. In this study samples were stored frozen for no longer than 21 months. BAS 125 W has been stable in the frozen state on soil for up to 17 months while despropionyl was not stable in freezer storage. Despropionyl samples fortified at 1.00 ppm degraded to 0.7 % of their original concentration during 12 months of storage. Within the first 21 days of storage about 80% of despropionyl degraded. Table XII presents BAS 125 W and its despropionyl degradate's storage stability data.

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DT$_{50}$ Calculations: The concentrations were calculated by averaging the three replicates of each depth interval for each sampling period and then summing the depth interval averages. The summed concentration for each sampling period was then analyzed by nonlinear regression of the natural log of the concentration relative to time. Concentrations <0.01 were considered to be zero for purpose of regression calculation. Nonlinear regression and the calculation of DT$_{50}$ and DT$_{90}$ were determined from the following equation:

$$Ln\ C = ln\ C_0 - \alpha\ ln\ (1+\beta t),$$

where C_0, α, and β are solved for in sequence as unknowns, after transforming the concentrations. Dissipation times are then calculated by:

$$DT_{50} = [0.5^{-(1/\alpha)}-1]/\beta$$

$$DT_{90} = [0.1^{-(1/\alpha)}-1]/\beta$$

α and β are determined by usig Coplot Scientific Graphics Software.

Solution Movement: Graphical presentations of correlation between residue mobility and soil water recharge events were performed. Soil solution movement was calculated from the following algorithm:

$$\text{Surface layer} \quad \Delta\Theta = \sum_i^{t=1}\left[(P+SM+I)-(Q-ETc)\right]$$

$$\text{Subsurface layer} \quad\quad \Delta\Theta = \sum_i^{t=1}\left[Inf - RFc\right]$$

t	time [days]
Θ	soil matrix water content
P	precipitation
SM	snow melt (when the snow pack exists and the ambient temperature is . 32 °F)
I	irrigation
Q	runoff
ETc	evapotranspiration corrected for the crop (ETc = ET * Kc); with Kc = 0.64 to 0.84
Inf	infiltration
RFc	root extraction factor RFc = RF * c; c = 1.0

STUDY AUTHORS' DATA SUMMARY:

Soil Characterization: Tables V, VI, and VII of the study present the results of test site soil characterization (attached). Table 3. Presents soilc haracterization summary results.

Meteorological Conditions: Table 8 and 8a (New York site, pp. 61 through 73, Appendix B), 9c (California site, pp. 97 through 109), 10b, 10c, and 10d (Oregon site, pp. 120 through 122) of the study presents the meteorological data for the test period. Table 2 (attached p 55, Appendix B) presents environmental conditions at application time.

Chemical Analysis:

Application Verification and Zero Time Recoveries: The application verification (AV) recovery rates for the petri dish were from 82.6% to 113% (see attached Table I). The authors of the study explain the the variance in the recoveries as due to the variance in the petri dish technique. Zero-time core recovery data varied from 86% to 163% (see Table II, it is noted that based on EFED calculations the recoveries were 92%, 85%, and 123% for the NY, CA, and OR sites, respectively). The authors attributed the variation to a quick degradation of parent compound to despropionyl. If the BAS 125 W degradate was added to the parent residue it could contribute to higher zero-time recovery data but since despropionyl was not stable in a storage conditions it was detected only in a low levels (<0.034 ppm, close to MDLs) thus would not change the results.

Dissipation Rate: Table III presents registrant calculated soil DT_{50}, DT_{90}, α, β, and R^2 for BAS 125 W and despropionyl (KI-5376). For BAS 125 the soil DT_{50} were 8, 9, and 3 days, and for despropionyl they were 5, 7 (derived from 2 data points), and 1 day, from the NY, CA, and OR bare soil, respectively. Figures 1 through 3 present nonlinear regression graphs for BAS 125 W and despropionyl at all three sites.

Residue Mobility and Solution Movement: Table VIII through X present BAS 125 W soil residues. The data indicate that prohexadione calcium was not detected below 12 inches and was only detected in four instances at 6 to 12-inch depths (single replicates at concentration no more than 0.067 ppm, LOQ = <0.01 ppm). The authors' review of graphical display of soil residue data by depth, with time, and soil solution transport by depth, with time, implies that although soil solution leached past 48 inch rootzone, prohexadione calcium did not move past 12 inch soil depth..

Metabolite Formation: Table XI presents despropionyl degradate soil residues. Despropionyl was formed from prohexadione calcium immediately after its application and persisted for up to 21 days in the NY site (14 days in CA and 7 days in OR). Figure 11 presents graphically a formation and decline of the metabolite. KI-5376 highest single maximum concentration of 0.055 ppm was found at 2nd day after last application in the CA site. The metabolite was detected in the 0-3" soil cores only. The authors estimate the metabolite half life (DT_{50}) as not greater than 7 days (based on 2 data points, Table III see attached, see The Reviewer's Comments 2).

Degradation Pathway: The registrant proposed degradation pathway indicates that prohexadione calcium degrades to despropionyl which degrades further into tricarballylic acid and citric acid, both naturally occurring substances. The two acids are subsequently mineralized to CO_2.

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THE REVIEWER'S COMMENTS:

1. The table below presents the EFED caclulated prohexadione calcium field dissipation half-life values. The half-lives, defined as $T_{1/2} = (\ln 2)/k = 0.693/k$, were derived from linear ($\ln C_t = \ln C_0 - kt$) and nonlinear regression analysis ($C = a*e^{-kt}$) assuming first order kinetics, where the k values are the slopes of the regression lines.

Site	$t_{1/2}$ (days)[1]		$T_{1/2}$ (days)[2]	
NY bare soil	15	($r^2 = 0.76$)	52	($r^2 = 0.73$)
CA bare soil	20	($r^2 = 0.78$)	34	($r^2 = 0.64$)
OR bare soil	5.7	($r^2 = 0.89$)	47	($r^2 = 0.70$)

[1] $t_{1/2}$ derived from nonlinear regression
[2] $T_{1/2}$ derived from linear regression

   BAS 125 dissipated with the non-linear first order kinetics half-life of 15, 20 , and 5.7 days from bare ground soil in the NY, CA, and OR sites, respectively. The higher r^2 value was the criterion for selection of $t_{1/2}$ between the two obtained half-lives. The r^2 values were greater for nonlinear regression by 3- 19.

2. The half-lives in these field dissipation studies are longer than expected from the laboratory study findings (aerobic soil metabolism non-linear $T_{1/2} = 1.4$ days with $r^2 = 0.98$, linear $T_{1/2} = 9.8$ days with $r^2 = 0.73$; MRID 44457785) and longer than those of the field dissipation studies conducted in TX and NC (linear $T_{1/2}$ of 0.8 day, TX, and 1.0 day, NC, calculated after the 3rd field application, MRID 44457791). Most likely it is due to soil moisture deficit, in NY and CA sites in particular (see The Reviewers' Comments 4 and MRID 44457791: The Reviewers' Comments 2, 4 and 7), compared to the control moisture conditions in the laboratory studies. Additionally, the field data generated in these studies were very scattered (see Appendix 1 Figures 1 through 3) suggesting a collection of insufficient sample size to obtain representative data and/or not uniform prohexadione calcium application.

3. Prohexadione calcium residues were detected at a depth of 6-12" inches in the CA site (one replicate of 0.017 ppm at 10 days after 2nd application), in the OR site (two replicates of 0.067 ppm at 2 days after 1st application and 0.019 ppm at 10 days after 2nd application), and in the NY site (one replicate of 0.015 ppm at 1 day after 1st application). These concentrations are above the method LOQs (0.01 ppm) and thus are indicative of leaching as a possible route of prohexadione calcium dissipation. The residue detection immediately after treatment in the NY site, however, could be due to sample

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contamination not due to leaching. No residues were detected below 12 inches at concentrations $\geq$0.01 ppm.

4. The CA and NY studies does not provide useful quantitative data to assess the fate and transport of the degradate. To avoid loss of the degradate in the storage the samples supposed to be analyzed immediately after sampling. In most cases dyspropionyl concentrations were close to or below the LOQ values (0.01 ppm). Residues of despropionyl were detected at a maximum concentration of 0.055 ppm at the 0-3" inch depth at 2 days after the 2nd application in CA site. From the bare ground soil in the OR site despropionyl dissipated with an EFED calculated half-life of 14 days (r^2 = 0.73).

5. The environmental conditions data in the NY site (Table 6 and 8) showed that in August water evaporation was significantly greater than precipitation . This indicates a water deficit during the month of prohexadione calcium application, which could result in low soil moisture content and thus prohibit the compound from leaching. In CA site, in August the evapotranspiration amounts (ETo = 7.17 inches, Table 9c) were the same as the irrigation amounts (7.02 inches, Table 5) indicating water deficit. In both cases the irrigation should be more intense to prevent soil dryness. The study report indicated no water deficits in September.

month	NY					CA			
	Precip	Irrigat	Prec + Irrig	PPT hund ins	Pan Evap thou in	Precip	Irrigat	Prec + Irrig	ETo in
Aug 96	3.36	0.72	4.08	336	5986	0	7.02	7.02	7.17
Sep 96	6.25	0.65	6.9	625	3355	0	9.36	9.36	4.95
Oct 96	4.06	0	4.06	406	1621	1.12	4.68	5.8	2.9

6. The study authors proposed degradation route indicates that prohexadione calcium degrades to despropionyl which degrades further into tricarballylic acid and citric acid, both naturally occurring substances. The two acids are subsequently mineralized to CO_2.

REFERENCES

McCall P.J., Swann R.L., Laskowski D.A., Unger S.M., Vrona S. A. and Dishburger H.J. Estimation of Chemical Mobility in Soil from Liquid chromatographic Retention Times. 1980 Bull. *Environ. Contam. Toxicol.* **24**, pp190-195.
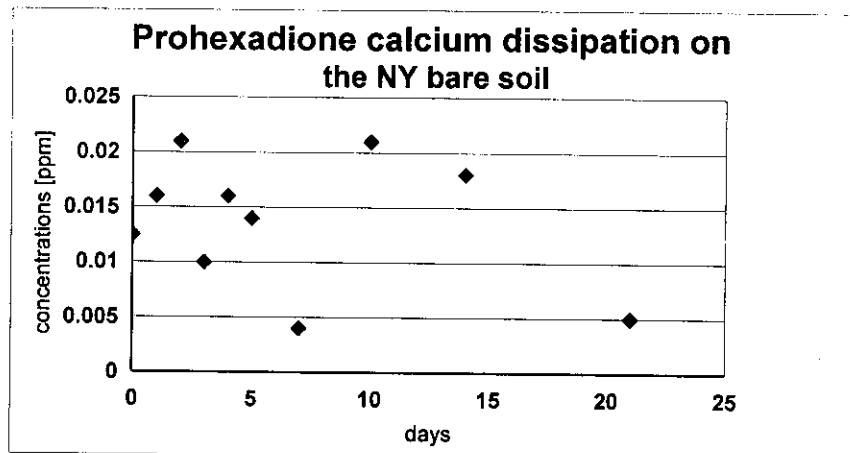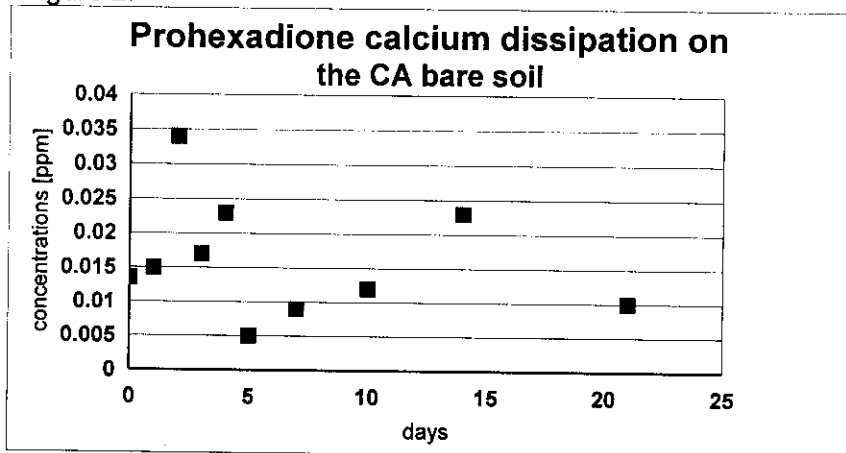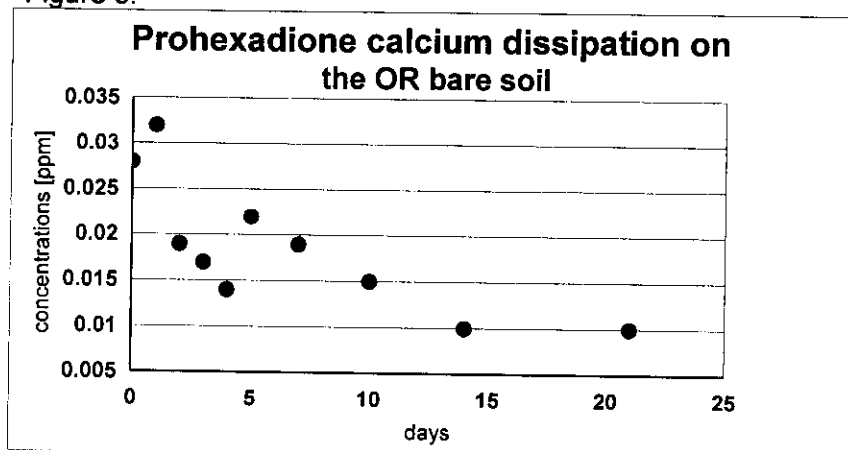
Figure 1.

Prohexadione calcium dissipation on the NY bare soil

Figure 2.

Prohexadione calcium dissipation on the CA bare soil

Figure 3.

Prohexadione calcium dissipation on the OR bare soil

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Pages 11 through 34 are not included.

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